

## REMARKS

### Status of the claims

Claims 1, 23-28, 30-48 and 52-57 were pending and Claims 1, 23, 24, 33-35, 38, 42-48 and 52 were withdrawn from consideration. Claim 30 has been amended as suggested to provide proper antecedent basis for the term "recognition helix" and claim 56 has been amended to eliminate redundant claim language. Claim 30 has also been amended to make explicit that at least one zinc coordinating residue is a cysteine and at least one is a histidine. See, e.g., page 19 and Example 4. In addition, claim 30 has also been amended to specify that there are 1, 2, 3, 4, 6 or 7 amino acid residues between the carboxy-terminal zinc coordinating residues (see, e.g., page 19 showing that the claimed non-canonical fingers have  $X_{1-7}$  residues between the carboxy-terminal zinc coordinating residues and Table 1 of the specification); that there are 2, 3 or 4 amino acids between the amino-terminal zinc coordinating residues (see, e.g., pages 19-20); and that there are at least 7 amino acids in the recognition helix (see, e.g. Table 3 of the specification as well as pages 19-20). Claim 56 has been amended to specify that there are 2 amino acid residues between the two amino-terminal zinc coordinating cysteine residues. See, e.g., pages 19-20 and Example 4 of the as-filed specification. Accordingly, claims 1, 23-28, 30-48 and 52-57 are pending as shown above and claims 25-28, 30-32, 36, 37, 39-41 and 53-57 under consideration.

### Restriction/Election

As previously acknowledged, the Restriction Requirement has been made Final. With regard to the remaining election of species requirements, Applicants again note that there upon indication that elected claim 30 is allowable, the withdrawn claims should be examined.

### Rejections Withdrawn

Applicants note that the rejections under 35 U.S.C. § 112, 1<sup>st</sup> paragraph (written description) have been withdrawn. (Office Action, page 4). In addition, the previous rejections under 35 U.S.C. § 103(a) have also been withdrawn.

**35 U.S.C. § 102(e)**

Claims 25-28, 30-32, 36, 37, 39-41 and 53-57 were newly rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 7,151,201 (hereinafter "Barbas"). (Office Action, pages 5-7). It was alleged that Barbas discloses "the use of plant C3H (CCCH) zinc finger proteins as a framework or backbone for the encoded polypeptide." (Office Action, page 6).

Applicants strongly traverse the rejection and supporting remarks.

The examined claims are directed to polynucleotides encoding zinc finger domains in which there are 1, 2, 3, 4, 6 or 7 residues between the carboxy-terminal zinc coordinating residues (claim 30 and claims dependent therefore) or in which there are 2 amino acids between the two amino zinc coordinating cysteine residues (claim 56 and claims dependent therefrom).

Barbas fails entirely to describe or demonstrate the claimed molecules. As a threshold matter, it is noted that Barbas contains a single phrase about C3H zinc finger proteins (Barbas at col. 22, lines 61-66):

In another specific embodiment, the zinc finger protein used in the present methods comprises a framework (or backbone) derived from a zinc finger protein that is naturally functional in plant cells. For example, the zinc finger protein used in the present methods can comprise a C3H zinc finger (Terol et al., *Gene*, 260(1-2):45-53 (2000)), ...

Notably, Barbas requires that the C3H zinc finger be functional in plants. However, no data is provided in Barbas as to C3H proteins modified in their recognition helix region, let alone whether such modified proteins would actually bind to a sequence in plant cell.

Moreover, the sole reference given by Barbas (Terol et al. (2000), attached hereto as Appendix A) is entirely speculative as to the function of the putative zinc finger (Terol, Abstract, pages 51, right column and page 52, left column, emphasis added):

Our data suggest an important role for these proteins. Based on the high sequence conservation within the conserved domains, we suggest that these proteins could have a regulatory function. ...

We consider that the ZFWD proteins might be a novel subfamily of proteins...we propose that they could have a regulatory role in plants. ...

The high degree of conservation found in very distant species supports the idea of an important role for the ZFWD proteins. The nature of this role will have to be addressed with further investigation.

Absolutely no evidence is provided in Barbas (or Terol) that the disclosed CCCH zinc finger binds DNA or has any function at all in the context of the naturally occurring protein. Certainly then, there is no disclosure that this CCCH zinc finger of unknown function could be isolated from its natural context, be modified to include an engineered recognition helix and still retain its unknown function. Thus, Barbas, by reference to Terol, fails to teach zinc finger proteins that are naturally functional in plant cells.

Furthermore, as acknowledged by the Office, Barbas refers only to CCCH proteins (as disclosed in Terol) having 7 amino acids between the amino terminal cysteines. As independent claim 30 requires that there be 2, 3 or 4 residues between the amino terminal zinc coordinating residues as well as at least 7 amino acids in the recognition helix region, Barbas disclosure of a specific CX<sub>7</sub>C X<sub>3</sub>C X<sub>3</sub>H finger cannot anticipate any of claims 25-28, 30-32, 36, 37, 39-41 and 53-57.

Similarly, independent claim 56 requires that there be 2 amino acid residues between the two amino terminal zinc coordinating cysteine residues. Barbas teaches (via reference to Terol) CCCH proteins having 7 residues between the amino terminal cysteine residues. See, Figure 2 of Terol. There is no teaching whatsoever in Barbas itself (or by reference to Terol) that the number of residues between the amino terminal cysteines should be modified (deleted) to make molecules as claimed (and, indeed, such modifications would be expected to render the zinc finger domain non-functional).

Thus, Barbas does not describe or demonstrate the claimed molecules and the rejection should be withdrawn.

35 U.S.C. § 103

Barbas

Claims 25-28, 30-32, 36-37, 39-41 and 53-57 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Barbas in view of Jiang et al. (Ref. No. C4 of IDS filed April 15, 2003, hereinafter "Jiang"). (Office Action, pages 8-10). Barbas is cited for teaching the elements of the claims except an isolated polynucleotide as claimed and Jiang is cited for teaching a C3H protein).

For the reasons noted above, Barbas (by reference to Terol) fails to teach non-canonical zinc finger domains set forth in claims 30 and claims dependent therefrom, namely zinc fingers having 2-4 amino acid residues between the amino terminal zinc coordinating residues and 1, 2, 3, 4, 6 or 7 amino acid residues between the carboxy terminal zinc coordinating residues. Jiang fails to cure Barbas's deficiency as it teaches only CCHC fingers, which necessarily have 5 amino acid residues between the carboxy terminal histidine and cysteine residues. Moreover, as there are absolutely no teachings in Barbas, Terol or Jiang to modify the number of residues between the carboxy terminal zinc coordinating residues, there is no combination of Barbas and Jiang that would result in the molecules of claims 25-28, 30, 31, 32, 36, 37, 39-41 and 53-55.

With regard to claims 56 and 57, Barbas fails entirely to teach or suggest CCCH zinc fingers having 2 amino acid residues between the amino terminal zinc coordinating residues. In fact, as noted above, the single CCCH zinc finger as disclosed in Barbas (via Terol) includes 7 amino acid residues in this region. Furthermore, as Barbas clearly teaches only modification of the recognition helix (which lies between the 2<sup>nd</sup> and 3<sup>rd</sup> zinc coordinating residues), there is no combination of Barbas and Jiang that would ever result in the claimed subject matter.

For at least the foregoing reasons, withdrawal of the rejection is in order.

Barbas II: claims 25-28, 30-32, 36-37, 39-41 and 53-57

Claims 25-28, 30-32, 36-37, 39-41 and 53-57 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,242,568 (hereinafter "Barbas II") in view of Jiang. (Office Action, pages 10-13). In addition, claim 37 was rejected as

allegedly obvious over Barbas II in view of Jiang and in further view of Guyer, which was cited as previously for allegedly disclosing GAL4-C1 fusion proteins. (Office Action, pages 13-15). Claims 25-28, 30-32, 36, 39-41 and 53-55 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Barbas II in view of Hori. (Office Action, pages 15-18). Claim 37 was rejected as allegedly obvious over Barbas II in view of Hori and in further view of Guyer. (Office Action, pages 18-19).

While it was acknowledged that Barbas II does not teach isolated polynucleotides encoding a non-canonical zinc finger protein, Jiang and Hori were alleged to teach this element. (Office Action, pages 12 and 16).

For the reasons noted above, Jiang fails to cure the admitted deficiency of Barbas II, namely that Barbas II does not in any way teach non-canonical zinc fingers as claimed. In particular, Jiang does not teach zinc finger proteins with the recited number of amino acid residues between the carboxy and amino terminal zinc coordinating residues.

Similarly, Hori teaches only H4 fingers, which, like C4 zinc finger proteins, are excluded from the scope of pending claims 25-28, 30-32, 36-37, 39-41 and 53-57 (which require that at least one of the four zinc coordinating residues is a cysteine residue).

Further, Guyer teaches a hybrid transcription factor comprising the DNA binding domain of the *S. cerevisiae* GAL4 protein and the transcription activation domain of the maize C1. There is no discussion of non-canonical zinc finger components as claimed. Accordingly, Guyer fails to cure the deficiencies of Barbas, Jiang and Hori.

Thus, a *prima facie* case of obviousness has not been and cannot be established and the rejections should be withdrawn.

Barbas II – claims 56 and 57

Claims 56 and 57 were rejected as allegedly obvious over Barbas II in view of Hori and further in view of Jiang. (Office Action, pages 19-22).

As acknowledged, Barbas does not teach or suggest non-canonical zinc finger proteins as set forth in claims 56 and 57. Hori also fails entirely to teach or suggest a non-canonical zinc finger in which the 2 amino terminal zinc coordinating are cysteine

residues. Rather, Hori discloses only canonical Sp1 or histidine-only H4 Sp1 fingers, which are excluded from the scope of claims 56 and 57. Jiang also fails to teach or suggest non-canonical zinc finger proteins as claimed in which there are 2 amino acids between the amino terminal cysteine zinc coordinating residues. Guyer is similarly deficient for the reasons of record and reiterated above.

Thus, there is no combination of Barbas, Hori, Jiang and Guyer that can lead the skilled artisan to the non-canonical zinc finger proteins of the instant invention.


**CONCLUSION**

In light of the amendments and remarks presented herein, it is believed that the elected subject matter is in condition for allowance. Applicants therefore request examination of generic subject matter. If the Examiner believes that a telephone conversation would expedite prosecution, she is invited to contact the undersigned at the telephone number given below.

Respectfully submitted,

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By: \_\_\_\_\_



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